

**WHAT IS CLAIMED IS:**

1                   1.    A method for determining a genotype associated with increased or  
2   decreased resistance to familial bipolar affective disorder in a family affected by bipolar  
3   affective disorder, comprising:

4                       determining the genotype of at least one family member, wherein the  
5   genotype is determined with at least one marker for at least one chromosomal region linked  
6   to a locus associated with resistance to bipolar affective disorder, wherein the chromosomal  
7   regions are inclusive of and localized between *D4S402* and *D4S424*; inclusive of and  
8   localized between *D4S431* and *D4S404*; or inclusive and localized between *D11S394* and  
9   *D11S29*;

10                      determining, after the age of onset, the bipolar affective disorder disease  
11   status in the family member;

12                      comparing the genotype with the bipolar affective disorder disease  
13   status; and

14                      determining therefrom the genotype associated with increased or  
15   decreased resistance to bipolar affective disorder.

1                   2.    The method of claim 1, wherein the genotype is determined with  
2   markers for at least two of the chromosomal regions.

1                   3.    The method of claim 2, wherein the genotype is determined with  
2   markers for three of the chromosomal regions.

1                   4.    The method of claim 1, wherein the chromosomal region is inclusive of  
2   and localized between markers *D4S422* and *D4S1625*.

1                   5.    The method of claim 4, wherein the marker is *D4S175*, *D4S422*,  
2   *D4S1576*, *D4S2294*, *D4S1579*, *D4S397*, *D4S3089*, *D4S2965*, *D4S192*, *D4S420*, *D4S1644*,  
3   *D4S3334*, or combinations thereof.

1                   6. The method of claim 1, wherein the chromosomal region is inclusive of  
2 and localized between markers *D4S3007* and *D4S419*.

1                   7. The method of claim 6, wherein the marker is *D4S3007*, *D4S394*,  
2 *D4S2983*, *D4S2923*, *D4S615*, *AFM<sub>α</sub>184za9*, *D4S2928*, *D4S1065*, *D4S1582*, *D4S107*,  
3 *D4S3009*, *D4S2906*, *D4S2949*, *AFM087zg5*, *D4S2944*, *D4S403*, *D4S2942*, *D4S2984*,  
4 *D4S1602*, *D4S1511*, *D4S2311*, *D4S3048*, or combinations thereof.

1                   8. The method of claim 7, wherein the marker is *D4S3009*, *D4S2906*,  
2 *D4S2949*, *AFM087zg5*, *D4S2944*, *D4S403*, *D4S2942*, *D4S2984*, *D4S1602*, *D4S1511*,  
3 *D4S2311*, or combinations thereof.

1                   9. The method of claim 1, wherein the chromosomal region is inclusive of  
2 and localized between markers *D11S133* and *D11S29*.

1                   10. The method of claim 9, wherein the marker is *D11S133*, *D11S147*,  
2 *CD3D*, *D11S285*, *D11S29*, or combinations thereof.

1                   11. The method of claim 1, wherein the genotype at a single chromosomal  
2 region is determined with at least three markers.

1                   12. The method of claim 1, wherein the marker is for a restriction fragment  
2 length polymorphism or microsatellite polymorphism.

1                   13. A kit for determining a genotype associated with increased or decreased  
2 resistance to familial bipolar affective disorder, wherein the kit comprises markers for two or  
3 more of the chromosomal regions:

4                   inclusive of and localized between *D4S402* and *D4S424*;

5                   inclusive of and localized between *D4S431* and *D4S404*; and

6                   inclusive and localized between *D11S394* and *D11S29*.

1           14. The kit of claim 13, wherein the markers are selected from the group  
2 consisting of:

3                   *D4S175, D4S422, D4S1576, D4S2294, D4S1579, D4S397, D4S3089,*  
4 *D4S2965, D4S192, D4S420, D4S1644, D4S3334;*

5                   *D4S3007, D4S394, D4S2983, D4S2923, D4S615, AFM $\alpha$ 184za9,*  
6 *D4S2928, D4S1065, D4S1582, D4S107, D4S3009, D4S2906, D4S2949, AFM087zg5,*  
7 *D4S2944, D4S403, D4S2942, D4S2984, D4S1602, D4S1511, D4S2311, D4S3048; and*  
8 *D11S133, D11S147, CD3D, D11S285, D11S29.*

1           15. The method of claim 1, wherein the marker is amplified.

1           16. The method of claim 15, wherein the marker is amplified by the  
2 polymerase chain reaction.

1           17. The method of claim 1, wherein the presence or absence of an allele  
2 associated with increased resistance to bipolar affective disorder is determined.

1           18. The method of claim 1, wherein the genotype of an affected family  
2 member is determined.

1           19. The method of claim 1, wherein the genotype of a non-affected family  
2 member is determined.

1           20. The method of claim 1, further comprising:  
2                   determining the genotype of at least one family member, wherein the  
3 genotype is determined with at least one marker for at least one chromosomal region linked  
4 to a locus associated with susceptibility to bipolar affective disorder, wherein the  
5 chromosomal regions are inclusive of and localized between *D6S344* and *D6S89*; inclusive  
6 of and localized between *D13S171* and *D13S218*; or at about *D15S148*.

1           21. The method of claim 1, further comprising:

2                   determining the genotype of a tested individual from the affected  
3 family, wherein the genotype is determined with at least one marker for at least one  
4 chromosomal region linked to a locus associated with resistance to bipolar affective disorder,  
5 wherein the chromosomal regions are inclusive of and localized between *D4S402* and  
6 *D4S424*; inclusive of and localized between *D4S431* and *D4S404*; or inclusive and localized  
7 between *D11S133* and *D11S29*;

8                   comparing the genotype of the tested individual to the genotype  
9 associated with increased or decreased resistance to bipolar affective disorder; and  
10                   determining therefrom the increased or decreased risk of the tested  
11 individual developing familial bipolar affective disorder.

12           22. The method of claim 21, wherein the genotype of the tested individual is  
13 compared to the genotype of an affected family member.

14           23. A method for determining the contribution of a chromosomal region to  
1 the presence or absence of resistance to bipolar affective disorder in a family affected by  
2 bipolar affective disorder, comprising:

3                   determining the corresponding genotype of at least two family members,  
4 wherein the genotype is determined with at least one marker for at least one tested  
5 chromosomal region linked to a locus associated with resistance to bipolar affective disorder,  
6 wherein the tested chromosomal regions are inclusive of and localized between *D4S402* and  
7 *D4S424*; inclusive of and localized between *D4S431* and *D4S404*; or inclusive and localized  
8 between *D11S133* and *D11S29*;

9                   determining, after the age of onset, the bipolar affective disorder disease  
10 status in the family members;

11                   comparing the genotypes of the family members; and

12                   determining therefrom the contribution of the chromosomal region to  
13 the presence or absence of resistance to bipolar affective disorder in the family.  
14

1           24. A method for determining a genotype associated with increased or  
2 decreased resistance to familial bipolar affective disorder in a family affected by bipolar  
3 affective disorder, comprising:

4                   determining the genotype of at least one family member, wherein the  
5 genotype is determined with at least one marker for at least one chromosomal region linked  
6 to a locus associated with resistance to bipolar affective disorder, wherein the chromosomal  
7 regions are inclusive of and localized between *D4S402* and *D4S424*; inclusive of and  
8 localized between *D4S431* and *D4S404*; or inclusive and localized between *D11S133* and  
9 *D11S29*;

10                   determining the genotype of at least one family member, wherein the  
11 genotype is determined with at least one marker for at least one chromosomal region linked  
12 to a locus associated with susceptibility to bipolar affective disorder, wherein the  
13 chromosomal regions are inclusive of and localized between *D6S344* and *D6S89*; inclusive  
14 of and localized between *D13S171* and *D13S218*; or at about *D15S148*;

15                   determining, after the age of onset, the bipolar affective disorder disease  
16 status in the family member;

17                   comparing the genotype with the bipolar affective disorder disease  
18 status; and

19                   determining therefrom the genotype associated with increased or  
20 decreased resistance to bipolar affective disorder.

1           25. The method of claim 24, wherein the marker associated with  
2 susceptibility is *D6S7*, *D13S1*, *D15S45*, or combinations thereof.

1           26. The method of claim 24, further comprising:  
2                   determining the genotype of a tested individual from the affected  
3 family, wherein the genotype is determined with at least one marker for at least one  
4 chromosomal region linked to a locus associated with resistance to bipolar affective disorder,  
5 wherein the chromosomal regions are inclusive of and localized between *D4S402* and

6 *D4S424*; inclusive of and localized between *D4S431* and *D4S404*; or inclusive and localized  
7 between *D11S133* and *D11S29*;

8 comparing the genotype of the tested individual to the genotype  
9 associated with increased or decreased resistance to bipolar affective disorder; and

10 determining therefrom the increased or decreased risk of the tested  
11 individual developing familial bipolar affective disorder.

1 27. A kit comprising markers D6S7, D13S1, or D15S45 for performing the  
2 method of claim 24.

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